Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A ~~biologically active~~ polypeptide having the amino acid sequence consisting essentially of AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04} (SEQ ID NO:1), wherein:

X_{01} is Ala, Asp or Gln;

X_{02} is Leu, Arg or homoArg;

X_{03} is Arg or Ala; [[and]]

X_{04} is Phe or Trp; and

wherein said polypeptide has a biological activity substantially similar to the biological activity of parathyroid hormone.

2. (cancelled).

3. (withdrawn) A polypeptide comprising an amino acid sequence consisting essentially of AlaValAlaGluIleGlnLeuMetHisX_{01}ArgAlaLysX_{02} (SEQ ID NO:2), wherein :

X_{01} is Ala, Asp or Gln; and

X_{02} is Trp or His.

4. (withdrawn) A polypeptide having an amino acid sequence that is at least 85% identical to the amino acid sequence of the polypeptide of claim 3.

5. (withdrawn) A polypeptide comprising the amino acid sequence: AlaValAla GluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetX_{05}Arg (SEQ ID NO:25), AlaValAla GluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetX_{05}ArgValGlu (SEQ ID NO:26), AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetX_{05}ArgValGluTrpLeu (SEQ ID NO:27) AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetX_{05}ArgValGlu TrpLeuArgLys (SEQ ID NO:28), AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsn SerMetX_{05}ArgValGluTrpLeuArgLysLysLeu (SEQ ID NO:29), AlaValAlaGluIleGlnLeuMet His$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetX_{05}ArgValGluTrpLeuArgLysLysLeuGlnAsp (SEQ ID NO:30), or AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}AsnSerMetX_{05}ArgValGluTrp LeuArgLysLysLeuGlnAspValHis (SEQ ID NO:31) wherein:

X_{01} is Ala, Asp or Gln;

X_{02} is Leu, Arg or homoArg;

X_{03} is Arg or Ala;

X_{04} is Phe or Trp; and

X_{05} is Arg or Ala.

6. (withdrawn) A polypeptide having an amino acid sequence that is at least 90% identical to the amino acid sequence of the polypeptide of claim 5.

7. (withdrawn) A polypeptide having an amino acid sequence selected from the group of sequences consisting of: AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHis (SEQ ID No:3), AlaValSerGluIleGlnLeuMetHisAsnArgGlyLysHis (SEQ ID No:4), AlaValSerGluIle GlnLeuMetHisAsnArgAlaLysHis (SEQ ID No:5), AlaValAlaGluIleGlnLeuMetHisAsnArg AlaLysHis (SEQ ID No:6), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysTrp (SEQ ID

No:7), AlaValAlaGluIleGlnLeuMetHisGlnArgAlaLysHis (SEQ ID No:8), AlaValAlaGluIle GlnLeuMetHisAlaArgAlaLys (SEQ ID No:9), AlaValAlaGluIleGlnLeuMetHisAlaArgAla (SEQ ID No:10), AlaValAlaGluIleGlnLeuMetHisAlaArg (SEQ ID No:11), AlaValAlaGluIle GlnLeuMetHisAlaArgAlaLysHisLeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGln AspValHisAspTyr (SEQ ID No:12) and AlaValSerGluIleGlnLeuMetHisAlaArgAlaLysHis (SEQ ID No:13), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuAlaSerValGluArg MetGlnTrpLeuArgLysLysLeuGlnAspValHisAspTyr (SEQ ID No:20), AlaValAlaGluIleGln LeuMetHisAlaArgAlaLysHisLeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGlnAsp ValHisAspTyr (SEQ ID No:22), AlaValAlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuAla SerValArgArgMetGlnTrpLeuArgLysLysLeuGlnAspValHisAspTyr (SEQ ID No:23) AlaVal AlaGluIleGlnLeuMetHisAlaArgAlaLysHisLeuAsnSerMetArgArgValGluTrpLeuArgLysLys LeuGlnAspValHisAspTyr (SEQ ID No:24)

8. (previously presented) The biologically active polypeptide of claim 1, wherein said polypeptide contains a C-terminal amide.

9. (cancelled).

10. (currently amended) The ~~biologically active~~ polypeptide of claim 1 wherein said peptide is labeled with a label selected from the group consisting of: a radiolabel, a fluorescent label, a bioluminescent label, or a chemiluminescent label.

11. (currently amended) The ~~biologically active~~ polypeptide of claim 10, wherein said radiolabel is ^{99m}Tc.

12. (currently amended) A pharmaceutical composition comprising: the ~~biologically active~~ polypeptide of claim 1; and a pharmaceutically acceptable carrier.

13. (withdrawn) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the polypeptide of claim 1.

14. (withdrawn) An isolated nucleic acid molecule comprising a nucleotide sequence encoding the polypeptide of claim 7.

15. (withdrawn) A recombinant DNA molecule comprising: (1) an expression control region, said region operably linked to (2) a polynucleotide sequence coding for the polypeptide of claim 1.

16. (withdrawn) A method of preparing a polypeptide, comprising introducing the nucleic acid of claim 13 into a host and expressing the polypeptide encoded by said nucleic acid.

17. (withdrawn) A method for making a recombinant vector comprising inserting a nucleic acid molecule of claim 13 into a vector.

18. (withdrawn) The recombinant DNA molecule of claim 15, wherein said control region includes a bacterial, viral, fungal or mammalian promoter.

19. (withdrawn) A prokaryotic or eukaryotic host cell containing the recombinant DNA molecule of claim 15.

20. (withdrawn) The cell of claim 19 which is bacterial.

21. (withdrawn) The cell of claim 19 which is a yeast cell or a mammalian cell.

22. (withdrawn) A polypeptide having the amino acid sequence of SEQ ID NO:14, wherein a single amino acid substitution reduces cAMP stimulation relative to the native PTH in HKRK-B7 cells, provided that said substitution is not alanine at any position, the substitution at Ser-1 is not Tyr, Pro or Asp, the substitution at Val-2 is not Leu, Ser, Arg or Glu, the substitution at Ser-3 is not Thr, Gly, Ile, or Asn and the substitution at Glu-4 is not Gly, His, Lys, Val or Asp.

23. (withdrawn) A polypeptide having the amino acid sequence of SEQ ID NO:14, wherein a single amino acid substitution increases cAMP stimulation in HKRK-B7 cells relative to the native PTH polypeptide, provided that said substitution is not alanine.

24. (withdrawn) The polypeptide of claim 21 wherein said single amino acid substitution is selected from the group consisting of:

(a) Asn-10 -->Asp, Glu or Gln;

(b) Leu-11 --> Ile, Met, Lys, Arg or Trp;

(c) Gly-12 -->Arg or His;

(d) Lys-13 -->Leu, Arg, His or Trp; and

(e) His-14 -->Leu, Arg, Phe or Trp.

25. (withdrawn) The polypeptide of claim 21, wherein said polypeptide contains amino acids 1-9, 1-10, 1-11, 1-12 or 1-13.

26. (withdrawn) A polypeptide selected from the group consisting of: PTH (1-20), PTH (1-22), PTH (1-24), PTH (1-26), PTH (1-28), PTH (1-30), PTH (1-32) and PTH(1-34),

wherein a single amino acid substitution increases cAMP stimulation in HKRK-B7 cells relative to the native PTH polypeptide, provided that said substitution is not alanine.

27. (withdrawn) The polypeptide of claim 25 wherein said single amino acid substitution is selected from the group consisting of:

(a) Asn-10 -->Asp, Glu or Gln;

(b) Leu-11 --> Ile, Met, Lys, Arg or Trp;

(c) Gly-12 -->Arg or His;

(d) Lys-13 -->Leu, Arg, His or Trp; and

(e) His-14 -->Leu, Arg, Phe or Trp.

(f) Glu-19 -->Arg

28. (withdrawn) The polypeptide of claim 21, wherein said polypeptide contains amino acids 1-9, 1-10, 1-11, 1-12, 1-13, 1-14, 1-20, 1-22, 1-24, 1-26, 1-28, 1-30, or 1-32.

29. (withdrawn) A method for treating mammalian conditions characterized by decreases in bone mass, wherein said method comprises administering to a subject in need thereof an effective bone mass-increasing amount of the polypeptide of any one of claims 1.

30. (withdrawn) A method for determining rates of bone reformation, bone resorption and/or bone remodeling comprising administering to a patient an effective amount of a polypeptide of any one of claims 1 and determining the uptake of said peptide into the bone of said patient.

31. (withdrawn) The method of claim 29, wherein said effective bone mass-increasing amount of said peptide is administered by providing to the patient DNA encoding said peptide and expressing said peptide *in vivo*.

32. (withdrawn) The method of claim 29, wherein the condition to be treated is osteoporosis.

33. (withdrawn) The method of claim 32, wherein said osteoporosis is old age osteoporosis.

34. (withdrawn) The method of claim 32, wherein said osteoporosis is post-menopausal osteoporosis.

35. (withdrawn) The method of claim 29, wherein the effective amount of said polypeptide for increasing bone mass is from about 0.01 μg/kg/day to about 1.0 μg/kg/day.

36. (withdrawn) The method of claim 29, wherein the method of administration is parenteral.

37. (withdrawn) The method of claim 29, wherein the method of administration is subcutaneous.

38. (withdrawn) The method of claim 29, wherein the method of administration is nasal insufflation.

39. (withdrawn) A method of increasing cAMP in a mammalian cell having PTH-1 receptors, comprising contacting said cell with a sufficient amount of the polypeptide of claim 1 to increase cAMP in said cell.

40. (withdrawn) A polypeptide having the amino acid sequence AlaValAlaGluIleGln LeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAsnSerMetGluArgValGluTrpLeuArgLysLysLeuGlnAspVal HisAspX_{05} (SEQ ID NO:16) or SerValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04}LeuAlaSer ValGluMetGlnGluTrpLeuArgLysLysLeuGlnAspValHisAspX_{05} (SEQ ID NO:21), wherein X_{01} is Ala Asp;

X_{02} is Leu or Arg;

X_{03} is Arg or Ala; X_{04} is Phe or Trp; and

X_{05} is Phe or Tyr.

41. (withdrawn) A method of increasing inositol phosphate in a mammalian cell having PTH-1 receptors, comprising contacting said cell with a sufficient amount of the polypeptide of claim 1 to increase inositol phosphate in said cell.

42. (currently amended) A ~~biologically active~~ polypeptide having an amino acid sequence, said sequence consisting essentially of a sequence selected from the group consisting of:

(a) AlaValAlaGluIleGlnLeuMetHis$X_{01}X_{02}X_{03}$LysX_{04} (SEQ ID NO:1);

(b) N- or C- derivatives thereof; and

(c) fragments containing amino acids 1-9, 1-10, 1-11, 1-12 or 1-13 thereof;

wherein: X_{01} is Ala, Asp or Gln;

X_{02} is Leu, Arg or homoArg;

X_{03} is Arg or Ala; and

X_{04} is Phe or Trp;

and wherein said polypeptide has a biological activity substantially similar to the biological activity of parathyroid hormone.